A guide to investigating hypertension in pregnancy

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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Hypertension can affect between 3 and 10% of all pregnancies. The Australasian Society for the Study of Hypertension in Pregnancy consensus statement defines hypertension in pregnancy as a systolic blood pressure greater than or equal to 140 mmHg and/or a diastolic blood pressure (taken as Korotkoff sound V) above or equal to 90 mmHg.[1]

Classification of hypertension in pregnancy

Gestational hypertension

Gestational hypertension is defined as an increase in blood pressure to greater than or equal to 140/90 mmHg after 20 weeks' gestation that resolves within three months postpartum in a woman with no previous history of renal disease or hypertension before the pregnancy.

Pre-eclampsia

Hypertension in pregnancy that occurs after 20 weeks' gestation is termed pre-eclampsia if it is associated with at least one of the following:

- proteinuria equal to or above 300 mg/24 hours or urinary albumin:creatinine ratio above 30 mg/mmol
- renal insufficiency, a serum creatinine greater than or equal to 90 μmol/L or oliguria
- raised serum transaminases and/or severe epigastric or right upper quadrant pain
- neurological complications of convulsions, hyper-reflexia with clonus, or persistent visual disturbances
- thrombocytopenia
- haemolysis
- disseminated intravascular coagulation (DIC)
- fetal growth restriction.

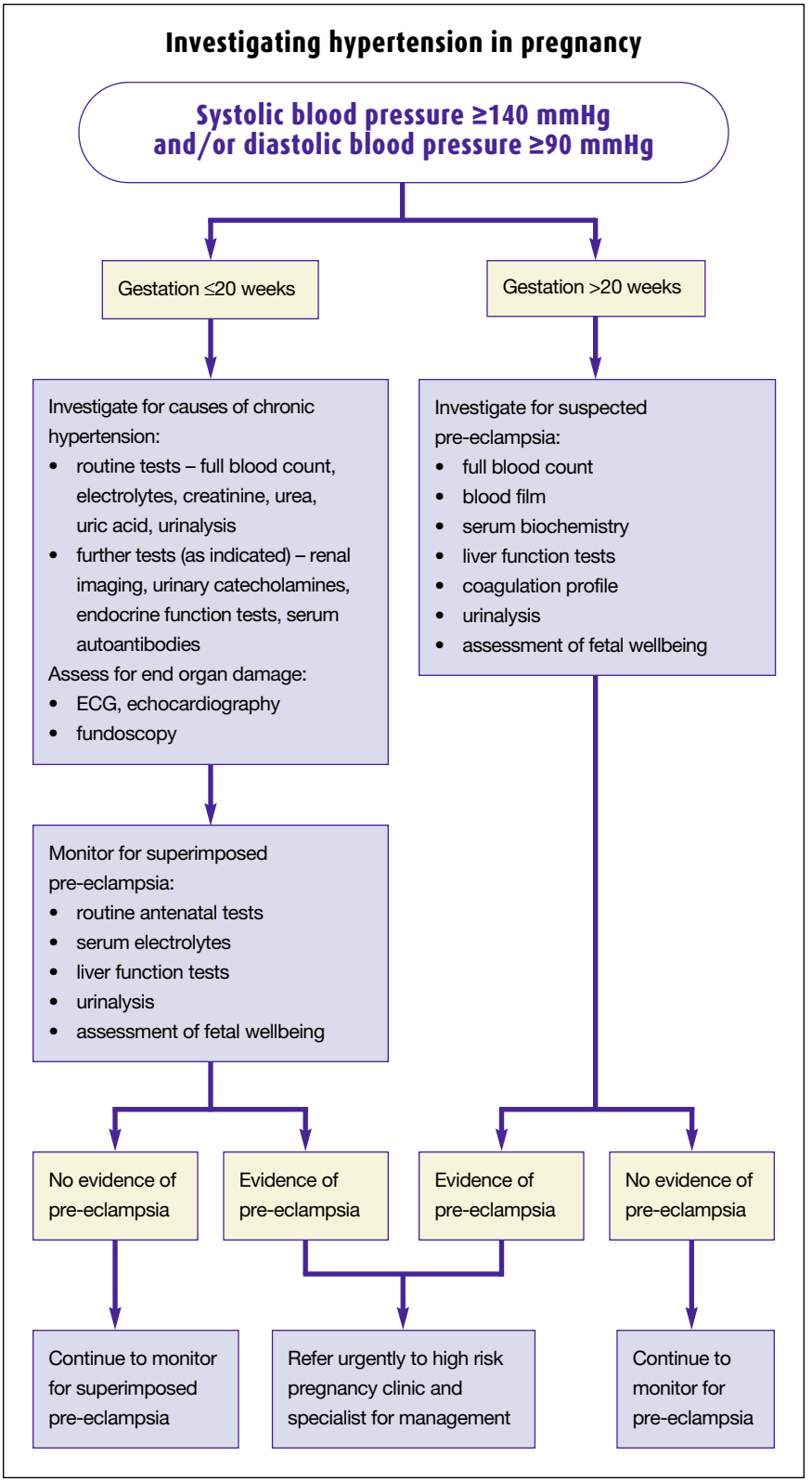
By definition, both pre-eclampsia and gestational hypertension resolve within three months postpartum.

Chronic hypertension (essential and secondary)

Chronic hypertension is defined as blood pressure elevated above 140/90 mmHg either before conception or before 20 weeks' gestation and not associated with any additional features indicative of pre-eclampsia.

IN SUMMARY

- **Hypertension can affect between 3 and 10% of all pregnancies.**
- **Hypertension in pregnancy is defined as a systolic blood pressure greater than or equal to 140 mmHg and/or diastolic blood pressure above or equal to 90 mmHg.**
- **Gestational hypertension is defined as onset of hypertension in pregnancy after 20 weeks' gestation in a woman with no previous history of renal disease or hypertension.**
- **Pre-eclampsia is defined as gestational hypertension associated with renal, hepatic, neurological or coagulopathic complications, or fetal growth restriction.**
- **Women with chronic hypertension should be monitored for the development of superimposed pre-eclampsia during pregnancy.**
- **Pre-eclampsia, by definition, resolves by three months postpartum.**



Chronic hypertension with superimposed pre-eclampsia

One or more of the features of pre-eclampsia may develop in patients with primary or secondary chronic hypertension, indicating pre-eclampsia that is superimposed on chronic hypertension. In patients who have underlying renal disease as a cause of their chronic hypertension, an increase in blood pressure and proteinuria may be difficult to interpret. Therefore, additional test results that indicate pre-eclampsia, such as elevated transaminases or thrombocytopenia, or other clinical signs and symptoms are required to aid the diagnosis.

Investigating hypertension in pregnancy

The flowchart on this page summarises the steps involved in investigating and monitoring a woman with hypertension during pregnancy.

Investigating suspected pre-eclampsia

Although blood pressure is the best clinical marker of pre-eclampsia, the presence of symptoms and abnormal blood tests may, independent of blood pressure, determine the need for urgent delivery and define the maternal risk.

In women who have developed hypertension after 20 weeks' gestation, the following investigations should be performed.

Electrolytes and uric acid

Glomerular filtration rate and renal blood flow increase during normal pregnancy with a reduction in normal range values for serum creatinine. In pre-eclampsia, renal blood flow decreases and renal insufficiency may develop. A rise in serum creatinine above 90 μmol/L is indicative of acute renal failure in pregnancy.

Elevated uric acid levels serve as a marker for pre-eclampsia. Normal levels range from 0.13 to 0.33 mmol/L in early pregnancy to 0.18 to 0.45 mmol/L at full term.[2] A definite increase of 0.12 mmol/L

or a level 0.06 mmol/L above a previously recorded baseline is suggested by Redman and colleagues as indicating hypertensive disease of pregnancy.[3] High uric acid levels can also be seen in normal twin or triplet pregnancies.

Liver function tests

Liver dysfunction is also seen in patients with pre-eclampsia. It is evidenced by elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Bilirubin concentration may also be elevated because of liver damage or haemolysis in women with pre-eclampsia. Mildly elevated alkaline phosphatase (ALP) levels are placental in origin and seen in normal pregnancy.

Full blood count and blood film

During normal pregnancy, a woman's platelet count may fall slightly as a result of haemodilution. Thrombocytopenia as a part of pre-eclampsia should be considered if there is more than a 30% decrease in the platelet count compared with a previous level.

Haemolysis can occur in the form of microangiopathic haemolytic anaemia. It is a result of diffuse vascular endothelial cell injury and indicates severe pre-eclampsia. Haemolysis is demonstrated in this setting by a blood film showing schistocytes and fragmentation of red cells and by increased serum lactate dehydrogenase, bilirubin and decreased haptoglobin levels.

Coagulation profile

Pre-eclampsia is associated with activation of the coagulation cascade and can lead to DIC (as demonstrated in the case study on this page). A coagulation profile should be done if thrombocytopenia or haemolysis is present. In DIC, as well as thrombocytopenia, there will be an elevated D-dimer, prolongation of the activated partial thromboplastin time (APTT) and prothrombin time, and decreased levels of fibrinogen.

Case study of a woman with pre-eclampsia

A 39-year-old woman attending an antenatal visit at 33 weeks' gestation had a blood pressure of 150/90 mmHg. Her past medical history included a caesarean section for an uncomplicated breech pregnancy at 38 weeks' gestation in 1984 and a caesarean section for pre-eclampsia in 1987. There was no requirement for antihypertensive medication in either pregnancy. There was no significant history of renal or cardiac disease and no history of hypertension between pregnancies. There was no family history of pre-eclampsia, and this pregnancy was with the same partner.

At the patient's 12-week antenatal visit, her blood pressure had been 140/90 mmHg with no proteinuria. By 30 weeks' gestation, her blood pressure was 150/100 mmHg and she had required treatment with 300 µg clonidine (Catapres) four times a day and, subsequently, twice daily 50 mg metoprolol.

At the antenatal visit at 33 weeks' gestation, her blood pressure was 150/90 mmHg in both arms and dipstick urinalysis showed '++++ protein'. The examination was otherwise normal. The patient had no symptoms of pre-eclampsia and fetal movements were present. Fundal height was consistent with dates. The provisional diagnosis was pre-eclampsia superimposed on chronic hypertension, on the basis of her high initial blood pressure and the escalation of hypertension in the presence of significant new proteinuria after 20 weeks' gestation.

Serum biochemistry revealed a creatinine concentration of 67 µmol/L (normal range, 50 to 110 µmol/L), uric acid 0.52 mmol/L (0.15 to 0.40 mmol/L), AST 109 U/L (normally below 40 U/L) and ALT 129 U/L (normally below 35 U/L). Haemoglobin was 110 g/L (normal range, 115 to 165 g/L), platelet count was 130 x 10^9/L (150 to 400 x 10^9/L) and the blood film was normal. She was referred and admitted to hospital where a cardiotocogram (CTG) showed no signs of fetal distress. Ultrasound scan showed a gestational age of 32.5 weeks, and normal liquor volume, heart action and umbilical artery ratios. The estimated fetal weight was 1813 g.

The patient was given intramuscular corticosteroid injections to enhance fetal lung maturation. Forty-eight hours later, she suddenly developed severe right upper quadrant pain in association with a blood pressure of 180/100 mmHg. Examination revealed hyper-reflexia, two beats of clonus and marked epigastric and right upper quadrant tenderness. She was given two intravenous doses of 5 mg hydralazine (Apresoline) and commenced on intravenous magnesium sulfate for seizure prophylaxis. Repeat blood testing showed an AST of 284 U/L, ALT 324 U/L, creatinine 67 µmol/L and platelet count of 154 x 10^9/L. She underwent a caesarean section and a live male infant was delivered with Apgar scores of 5, 8 and 9 at one, five and 10 minutes, respectively.

Post-delivery, the patient was asymptomatic and clinically stable; magnesium sulfate and antihypertensives were continued. Her platelet count fell to 53 x 10^9/L. There was evidence of DIC with an APTT of 37 seconds (normal range, 25 to 35 seconds), fibrinogen 4.0 g/L (1.5 to 4.9 g/L) and D-dimer 1.6 µg/mL (normally below 0.5 µg/mL). She was discharged 10 days post-delivery, not requiring antihypertensive medication and without further complications.

Urinary protein

A dipstick urinalysis is a screening test for proteinuria. If the dipstick shows at least '+ protein', further quantification is required. This can be done by a random albumin:creatinine ratio or a 24-hour urinary protein examination. An albumin:creatinine ratio above 30 mg/mmol equates to a level on the 24-hour urine test above 300 mg/24 hours and indicates pathological proteinuria.

Fetal wellbeing

Fetal wellbeing is assessed by experienced obstetric staff with clinical assessment, cardiotocograms and ultrasound scans.

Investigating chronic hypertension

Elevated blood pressure in a pregnant woman prior to 20 weeks' gestation indicates essential or chronic hypertension and it is important during pregnancy to consider secondary causes. These include primary intrinsic renal disease, and vascular anomalies such as renal artery stenosis and coarctation of the aorta. Endocrine disorders that cause hypertension include phaeochromocytoma, Cushing's syndrome, hyperaldosteronism and abnormal thyroid function. Hypertension may be secondary to connective tissue diseases, such as systemic lupus erythematosus. The following tests should be performed.

Dipstick urinalysis

A dipstick urinalysis tests for protein, blood and glucose, and is routinely performed at the first antenatal visit. If any findings are positive, a midstream urine sample should be sent for microscopy, culture, antibiotic sensitivity and examination for urinary sediment. Any proteinuria or haematuria should lead to a 24-hour urinary protein collection and determination of creatinine clearance.

Routine blood tests

A full blood count and serum urea, creatinine, electrolytes, blood sugar and uric acid levels should be measured and may suggest the next line of investigation.

Further tests

Renal disease may present as an increase in creatinine concentration in early pregnancy. Renal ultrasound in indicated if there is a history of childhood urinary tract infection or any current evidence of renal disease.

Renal artery stenosis is suggested by resistant hypertension with an early age at onset and abdominal bruit. Elevated plasma renin and aldosterone concentrations occur in pregnancy and are not sensitive screening tests for renal artery stenosis. Renal artery Doppler imaging is safe during pregnancy, but if inconclusive and the index of suspicion is high, a limited renal angiogram can be performed by an experienced radiologist.

Phaeochromocytomas are diagnosed by a high 24-hour urinary catecholamine excretion or elevated serum catecholamines. Adrenal ultrasound is safe in pregnancy. Other endocrine abnormalities may be detected by appropriate function tests. Connective tissue diseases can be determined by elevated autoantibodies in the presence of clinical signs.

The end organ effects of longstanding hypertension can be assessed by an ECG and echocardiography. Ophthalmic fundal examination should be performed in all cases.

Monitoring for pre-eclampsia

The risk of superimposed pre-eclampsia in a woman with primary or secondary hypertension during pregnancy is 30%. Therefore, regular assessment for pre-eclampsia should include serum electrolyte tests repeated at 20 to 24 weeks, 25 to 28 weeks, and 33 to 36 weeks as well as other routine antenatal tests. If any change in urine testing results at any time, a 24-hour urinary protein collection or albumin:creatinine ratio should be repeated. These women should be managed in a high risk pregnancy clinic and referred to a renal physician if there is evidence of underlying renal disease.

Postpartum follow up and investigation

All patients with pre-eclampsia or gestational hypertension should be followed up postpartum. Hypertension or proteinuria that persists beyond three months postpartum is suggestive of underlying secondary causes of pre-eclampsia and should be referred appropriately.

Pre-eclampsia and thrombophilia

In some patients with severe early-onset pre-eclampsia (defined by onset of pre-eclampsia before 34 weeks' gestation) there is an increased incidence of inherited thrombophilia.

There is evidence that this group of patients may be predisposed to developing pre-eclampsia because of abnormalities in haematological and immunological factors.[4] These patients should be screened for protein S deficiency, activated protein C resistance, antithrombin III deficiency, hyperhomocysteinaemia and hypercoagulability due to anticardiolipin antibodies. If any abnormalities arise, specialist advice should be sought, as there is controversy in the literature about

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LAURENT–CATHY, B.S.I.P, AUSCAPE

Hypertension in pregnancy is defined as a blood pressure greater than or equal to 140/90 mmHg.

the appropriate management in subsequent pregnancies.

Long term sequelae of pre-eclampsia

Pre-eclampsia is more common in patients with the metabolic risk factors of obesity, insulin resistance, diabetes and hypercholesterolaemia.[5] This group of women is at future risk of cardiac disease, and it is yet to be determined whether pre-eclampsia is itself an independent risk factor for cardiovascular disease. It is recommended that women with a history of pre-eclampsia and cardiovascular risk factors be followed up after pregnancy with annual blood pressure monitoring and treatment if above 140/90 mmHg. Annual cholesterol testing, fasting blood sugar levels, microalbuminuria and weight monitoring are also advised, along with smoking cessation advice.

Conclusion

A doctor treating a pregnant woman with hypertension should first try to establish whether the hypertension is gestational or chronic. Newly diagnosed chronic hypertension warrants investigation of the underlying cause and assessment of any target organ damage.

All women with hypertension during their pregnancy must be monitored closely for the development of pre-eclampsia, which may endanger the wellbeing of both the mother and the fetus. Indicators of pre-eclampsia in a pregnant woman with hypertension include renal insufficiency, proteinuria above 300 mg/24 hours, elevated serum transaminases, thrombocytopenia, neurological complications and fetal growth restriction. Women with pre-eclampsia should be referred urgently to a specialist and a high risk pregnancy clinic for management. MT

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